REMARKS

Current Status of Claims

Claims 24-39 are pending. Claims 1-23 were previously cancelled. Claims 32 and 37-39 are, at present, withdrawn from consideration. Claims 24-31 and 33-36 have been rejected. Claim 24 has been amended to more clearly describe the step of reducing, where present in the soluble protein solution, the amount of DNA and endotoxin in solution. Support for the amendments to claim 24 can be found throughout the specification, for example on page 7, lines 14-19.

Continuing Traverse of Restriction and Election Requirement

Applicants reiterate their traverse of the May 16, 2006 restriction requirement. The restriction/species election requirement is neither supported by U.S. law or USPTO procedure. See applicant's arguments in the responses of February 28, 2007 and June 16, 2006.

While it is clear that the restriction requirement has not been withdrawn, the Office Action does not make it clear that the restriction requirement has been made final. On page 2, the instant Office Action states that "the examiner is indeed maintaining the requirement, and may withdraw claims as appropriate, which do not encompass the elected species/subgenera" and "acknowledges that applicants have traversed the election requirement, and that applicants will ultimately have the right to petition the requirement." Applicants respectfully request a clear statement on the record that either 1) the election requirement has been withdrawn, or 2) that the election requirement has been made final and that the election requirement was timely traversed. Either statement will greatly assist Applicants in determining whether to petition the election requirement.

Further, the Examiner mischaracterizes what is claimed in the invention and which species is elected with traverse. The Examiner mistakenly alleges that Applicants have elected a method wherein the proteins are not purified. However, Applicants have elected a method of removing suspended particles from a soluble protein solution comprising filtering the soluble

protein solution through highly purified diatomaceous earth, thereby providing a clarified protein solution wherein the proteins are not further purified. See, Applicants election with traverse in the Response of June 16, 2006 to the Restriction Requirement. Accordingly, in contrast to the Examiner's assertions the claimed invention as elected with traverse provides for preparing a clarified protein solution (a "purified protein solution") comprising the recited steps without further purifying the protein. Therefore, the claimed invention is directed to a process of purifying a soluble protein in solution. Applicants submit that throughout the specification a method of purifying protein (soluble protein in solution) is disclosed. Claim 32 would be properly withdrawn in view of the above, however, withdrawal from examination of claims 37-39, directed to a method for removing suspended particles from a soluble protein solution and reciting a yield of the obtained soluble protein, is not justified. Therefore, accordingly Applicants submit that claims 37-39 are improperly withdrawn.

Obviousness-type Double Patenting Rejections

Applicants will address the [provisional] rejections of claims 24-25 under the judicially created doctrine of obviousness-type double patenting over claims 1-4 of US 6,995,246 and over claim 24 of co-pending application Serial No. 10/698,230, intending to submit a terminal disclaimer upon the indication of allowance of the currently pending claims.

Claims 24-31 and 33-36 clearly define the claimed subject matter as under 35 U.S.C. §112, second paragraph

Claims 24-31 and 33-36 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite. According to the Examiner, the claims are drawn to removing suspended particles from a solution, which according to the Examiner is an impossibility because a solution excludes a suspension. In response Applicants submit that one skilled in the art would recognize that a solution of soluble material may contain particulate matter which can be removed using the process of the claimed invention. In addition, the skilled artisan reading the specification would immediately understand the meaning of the claim term "soluble protein solution." The specification clearly

describes a soluble protein solution throughout. In fact an entire section of the specification (Section 5.1 Sources of Soluble Protein Solutions) is dedicated to describing such soluble protein solutions which includes lysates and secreted protein solutions. Also, throughout the specification and for example in the very first paragraph after introductory remarks about related applications, the claimed method is described as removing suspended particles from secreted protein solutions and lysates. Further, Applicants point out that claim 24, from which all claims depend, either directly or indirectly, include the limitation that the soluble protein solution is a lysate. One of skill in the art in view of the above would immediately understand that the soluble protein solution contains dissolved protein (soluble protein) and particular matter such as for example cell debris. Therefore, the skilled artisan would consider the lysate a soluble protein solution from which particulate matter (particles) may need to be removed. The claimed process removes such particulate matter from such soluble protein solution. Therefore, claims 24-31 and 33-36 clearly define the claimed subject matter under 35 U.S.C. §112, second paragraph, and withdrawal of the rejection is respectfully requested.

Claims 24-31 and 33-36 are non-obvious

a). The Rejection of Claims 24-31 and 33-36 under 35 U.S.C. §103 Fails to Address All Limitations of the Claims

Claims 24-31 and 33-36 remain rejected under 35 U.S.C. §103 as being unpatentable over Hsu (US 6,008,328) in view of Hennen (US 6,468,534) or Colpan (US 6,274,371). This obviousness rejection is improper for failing to address a positive limitation of the instant claims, therefore failing to state a prima facie case of obviousness. The instant claims all require a process "comprising the step of ..... filtering the soluble protein solution through **highly purified** diatomaceous earth, thereby providing a clarified soluble protein solution". The clear meaning of this limitation (and particularly the word "thereby") is that filtration through highly purified diatomaceous earth must be the step that provides a clarified soluble protein solution, and not some other filtration step. All of the references cited against the instant claims teach the use of [diatomaceous earth only as] a "filter aid", and require some other matrix for the actual filtration step.

Hsu et al disclose the use of a filter aid but do not teach or suggest using diotamaceous earth, let alone highly purified diatomaceous earth. Neither Hennen et al or Colpan et al correct this deficiency in Hsu et al to teach or suggest the use of **highly purified** diatomaceous earth. Hennen et al at best teach the use of Celite® as a filter aid. Standard Celite® is not a highly purified diatomaceous earth as is shown in the attached Exhibit A. Exhibit A is a copy of the web pages for Advanced Minerals found at http://www.advanceminerals.com/celpure.html, the company that sells both Celite® and Celpure®. In contrast to standard Celite®, Celpure® is an example of a highly purified diatomaceous earth as described in the currently pending application. Colpan et al teach the use of a diol modified diatomaceous earth to prepare plasmid DNA and thus also fails to teach or suggest the use of highly purified diatomaceous earth.

The Examiner responded to Applicants arguments that the diatomaceous earth disclosed by Hennen et al is Celite®, which is produced by a company that is in the business of producing filter aids. According to the Examiner the skilled artisan would expect that such company would make at least some effort at purifying their product. This assertion by the Examiner is made entirely on conjecture without any evidentiary support. In fact evidence is readily available that filtration aids are **not** routinely provided in the form of highly purified diatomaceous earth. In contrast, the attached Exhibit A clearly shows that the company selling diatomaceous earth for use in filter aids provides both "standard" diatomaceous earth (Celite®) and highly purified diatomaceous earth (Celpure®, as is disclosed in the present application as an example of highly purified diatomaceous earth). Exhibit A also clearly shows that highly purified diatomaceous earth (as in Celpure®) is distinct from standard diatomaceous earth for filtration aids sold as Celite® (as disclosed in Hennen et al).

Accordingly, none of the cited references, taken singly or combined, teach the instant limitation of a step of filtration with **highly purified** diatomaceous earth which results in a clarified soluble protein solution. The Examiner has failed to establish a prima facie case of obviousness, and this rejections should be withdrawn.

b). The Rejection of Claims 24-31, 34, and 36 under 35 U.S.C. §103 Fails to Address All Limitations of the Claims

Claims 24-31, 34, and 36 are rejected under 35 U.S.C. §103 as being unpatentable over Lander et al (US 2001/44136). This obviousness rejection is also improper for failing to address a positive limitation of the instant claims, therefore failing to state a prima facie case of obviousness. The instant claims all require a process "comprising the step of reducing, where present in the soluble protein solution, the amount of DNA and endotoxins in solution". The clear meaning of this limitation is that the claimed process prepares a soluble protein solution wherein the amount of DNA and endotoxins is reduced. In contrast, Lander et al disclose a process of purifying a plasmid DNA. In fact, Lander et al, discloses that the disclosed process meets the needs of "provid[ing] a methodology to prepare scalable, clinical grade DNA plasmid lots which are substantially free of host cell protein." See Lander et al at paragraph [0011]. A process of purifying plasmid DNA is opposite to the method of the claimed invention and in contrast to the above recited limitation of reducing the amount of DNA in solution as required in independent claim 24. Therefore, Lander et al fail to teach or suggest the claimed process of reducing the amount of DNA in a soluble protein solution and instead teach away from the claimed invention. The Examiner's assertions are based on the mistaken belief that the currently claimed method, as elected in response to the restriction requirement, is not directed to a method of purifying protein as discussed above. However, regardless whether or not the Examiner asserts that the claimed method is not a method of purifying a protein, the claimed method explicitly requires the reduction of DNA which is in contrast to purifying DNA as in Lander et al. For these reasons, the Examiner has failed to establish a prima facie case of obviousness, and this rejection should be withdrawn.

c). The Rejections of Claim 24 under 35 U.S.C. §103 Fails to Address All Limitations of the Claim

Claim 24 was rejected under 35 U.S.C. §103 as being unpatentable over Theodossiou, I. (Bioprocess Engineering **16**(3), 175-183, 1997) in view of Luo (US 6,365,147) or Marquet (US 5,561,064). Claim 24 was also rejected under 35 U.S.C. §103 as being unpatentable over Colpan

(6,274,371) in view of Theodossiou et al. These obviousness rejections are also improper for failing to address a positive limitation of the instant claims, therefore failing to state a prima facie case of obviousness. The instant claim 24 requires a process "comprising the step of reducing, where present in the soluble protein solution, the amount of DNA and endotoxins in solution". The clear meaning of this limitation is that the claimed process prepares a soluble protein solution wherein the amount of DNA and endotoxins is reduced. In contrast, each of the cited references Theodossiou et al , Luo et al, Marquet et al, and Colpan et al disclose a process of purifying (a plasmid) DNA. In fact, Theodossiou et al, cited in both rejections, discloses "that virtual complete removal of solids (99.4%) and protein (96.8%) was achieved, with a 8.2-fold purification of plasmid DNA." See the abstract in Theodossiou et al at page 175. A process of purifying (plasmid) DNA is opposite to the method of the claimed invention and in contrast to the above recited limitation of reducing the amount of DNA is solution as required in claim 24. Therefore, each of the cited references, either singly or in combination, fails to teach or suggest the claimed process of reducing the amount of DNA in a soluble protein solution. Instead the cited references teach away from the claimed invention of reducing the amount of DNA in the soluble protein solution. The Examiner's assertions are apparently based on the mistaken believe that the currently claimed method, as elected in response to the restriction requirement, is not directed to a method of purifying protein as discussed above. However, regardless whether or not the Examiner asserts that the claimed method is not a method of purifying a protein, the claimed method explicitly requires the reduction of DNA which is in contrast to purifying DNA as in each of the cited references. For these reasons, the Examiner has failed to establish a prima facie case of obviousness, and these rejections should be withdrawn.

In view of the above remarks, applicant believes the pending application is in condition for allowance.

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Respectfully submitted,

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